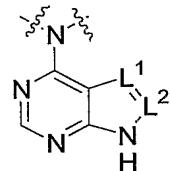


Claims

We claim:

- 5 1. A compound comprising one or more phosphonates and a substructure of formula I:



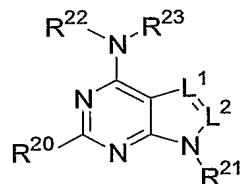
I

wherein L<sup>1</sup> and L<sup>2</sup> are -N- or -CR<sup>a</sup>-; and

R<sup>a</sup> is hydrogen, alkyl, substituted alkyl, aryl or substituted aryl;

10 or a pharmaceutically acceptable salt thereo.

2. The compound of claim 1 that comprises a substructure of the formula:



15 wherein:

L<sup>1</sup> and L<sup>2</sup> are independently -N-, or -CR<sup>a</sup>-, provided that only one of L<sup>1</sup> or L<sup>2</sup> is a nitrogen atom;

R<sup>a</sup> is hydrogen, alkyl, aryl or substituted aryl;

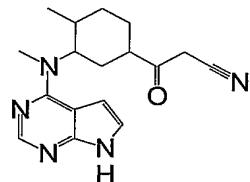
20 R<sup>20</sup> is hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl aryl, cycloalkyl, substituted aryl, or -NR<sup>b</sup>R<sup>c</sup>;

R<sup>b</sup> and R<sup>c</sup> are independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, or aralkyl;

R<sup>21</sup> is hydrogen, alkyl, cycloalkyl, substituted cycloalkyl, substituted alkyl, aryl, substituted aryl, aralkyl, or substituted aralkyl; and

$R^{22}$  and  $R^{23}$  are independently hydrogen, alkyl, substituted aryl, or aralkyl.

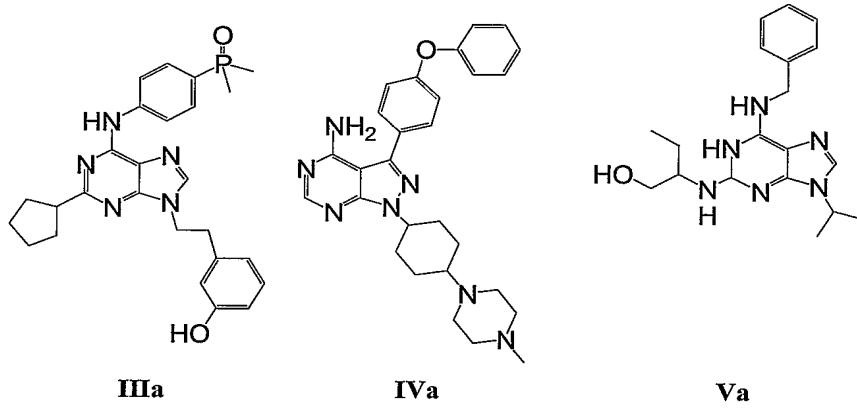
3. The compound of claim 1 that comprises a substructure of formula II:



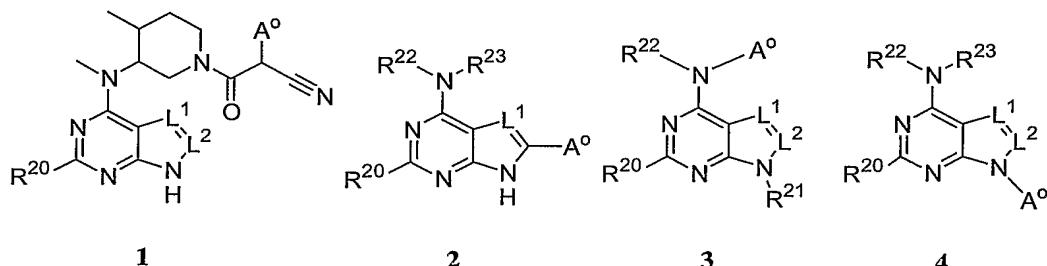
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II

4. The compound of claim 1 that comprises a substructure of formula IIIa, IVa or Va:



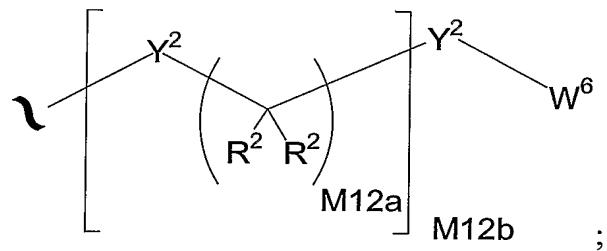
10 5. The compound of claim 1 having formula 1, 2, 3, or 4:



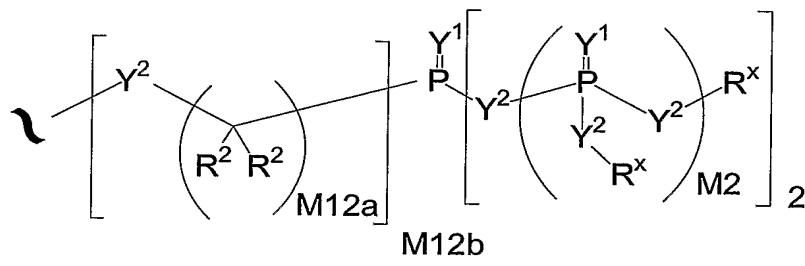
wherein:

$A^0$  is  $A^1$ ;

15  $A^1$  is:



$A^3$  is:



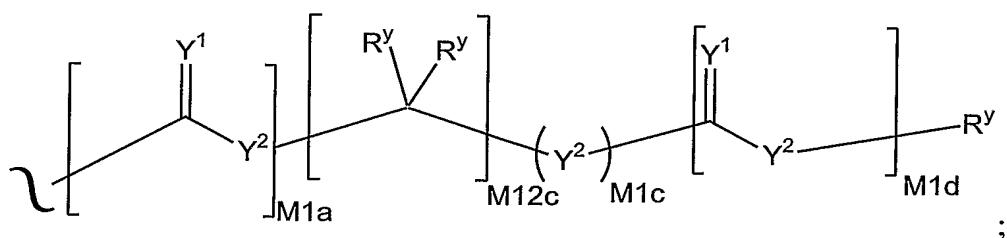
5

$Y^1$  is independently O, S, N( $R^x$ ), N( $OR^x$ ), or N(N( $R^x$ )( $R^x$ ));

$Y^2$  is independently a bond, O, N( $R^x$ ), N( $OR^x$ ), N(N( $R^x$ ))( $R^x$ )), or -

S(O) $M_2$ -; and when  $Y^2$  joins two phosphorous atoms  $Y^2$  can also be C( $R^2$ )( $R^2$ );

10             $R^x$  is independently H,  $R^2$ ,  $W^3$ , a protecting group, or the formula:



$R^y$  is independently H,  $W^3$ ,  $R^2$  or a protecting group;

$R^2$  is independently H,  $R^3$  or  $R^4$  wherein each  $R^4$  is independently

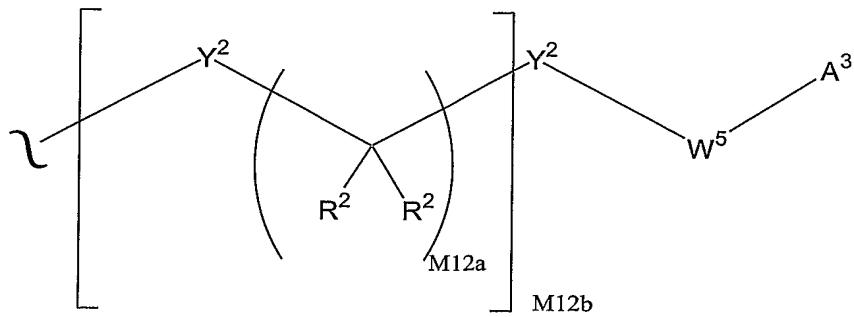
15            substituted with 0 to 3  $R^3$  groups;

$R^3$  is  $R^{3a}$ ,  $R^{3b}$ ,  $R^{3c}$  or  $R^{3d}$ , provided that when  $R^3$  is bound to a heteroatom, then  $R^3$  is  $R^{3c}$  or  $R^{3d}$ ;

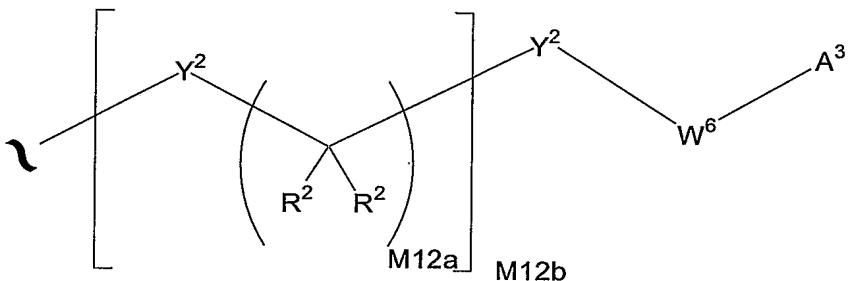
$R^{3a}$  is F, Cl, Br, I, -CN,  $N_3$  or -NO<sub>2</sub>;

$R^{3b}$  is  $Y^1$ ;

- $R^{3c}$  is  $-R^x$ ,  $-N(R^x)(R^x)$ ,  $-SR^x$ ,  $-S(O)R^x$ ,  $-S(O)_2R^x$ ,  $-S(O)(OR^x)$ ,  $-S(O)_2(OR^x)$ ,  $-OC(Y^1)R^x$ ,  $-OC(Y^1)OR^x$ ,  $-OC(Y^1)(N(R^x)(R^x))$ ,  $-SC(Y^1)R^x$ ,  $-SC(Y^1)OR^x$ ,  $-SC(Y^1)(N(R^x)(R^x))$ ,  $-N(R^x)C(Y^1)R^x$ ,  $-N(R^x)C(Y^1)OR^x$ , or  $-N(R^x)C(Y^1)(N(R^x)(R^x))$ ;
- 5  $R^{3d}$  is  $-C(Y^1)R^x$ ,  $-C(Y^1)OR^x$  or  $-C(Y^1)(N(R^x)(R^x))$ ;
- $R^4$  is an alkyl of 1 to 18 carbon atoms, alkenyl of 2 to 18 carbon atoms, or alkynyl of 2 to 18 carbon atoms;
- $R^5$  is  $R^4$  wherein each  $R^4$  is substituted with 0 to 3  $R^3$  groups;
- 10  $W^3$  is  $W^4$  or  $W^5$ ;
- $W^4$  is  $R^5$ ,  $-C(Y^1)R^5$ ,  $-C(Y^1)W^5$ ,  $-SO_2R^5$ , or  $-SO_2W^5$ ;
- $W^5$  is carbocycle or heterocycle wherein  $W^5$  is independently substituted with 0 to 3  $R^2$  groups;
- 15  $W^6$  is  $W^3$  independently substituted with 1, 2, or 3  $A^3$  groups;
- $M2$  is 0, 1 or 2;
- $M12a$  is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12;
- $M12b$  is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12;
- $M1a$ ,  $M1c$ , and  $M1d$  are independently 0 or 1;
- $M12c$  is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12;
- 20  $L^1$  and  $L^2$  are independently  $-N-$ , or  $-CR^a-$ , provided that only one of  $L^1$  or  $L^2$  is a nitrogen atom;
- $R^a$  is hydrogen, alkyl, aryl or substituted aryl;
- $R^{20}$  is hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl aryl, cycloalkyl, substituted aryl, or  $-NR^bR^c$ ;
- 25  $R^b$  and  $R^c$  are independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, or aralkyl;
- $R^{21}$  is hydrogen, alkyl, cycloalkyl, substituted cycloalkyl, substituted alkyl, aryl, substituted aryl, aralkyl, or substituted aralkyl; and
- $R^{22}$  and  $R^{23}$  are independently hydrogen, alkyl, substituted aryl, or aralkyl.
- 30 6. The compound of claim 5 wherein  $A^1$  is of the formula:

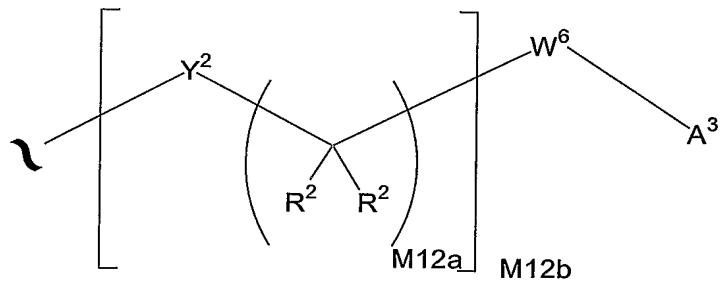


7. The compound of claim 5 wherein  $A^1$  is of the formula:

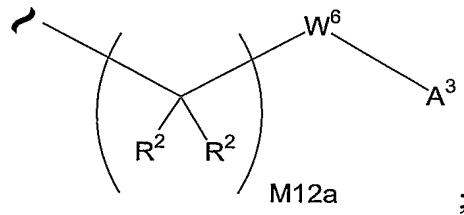


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8. The compound of claim 5 wherein  $A^1$  is of the formula:

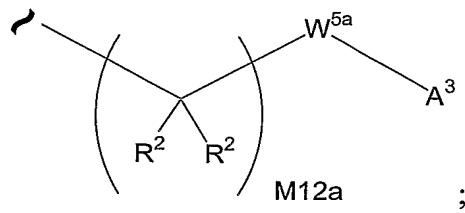


9. The compound of claim 5 wherein  $A^1$  is of the formula:



10

10. The compound of claim 5 wherein  $A^1$  is of the formula:

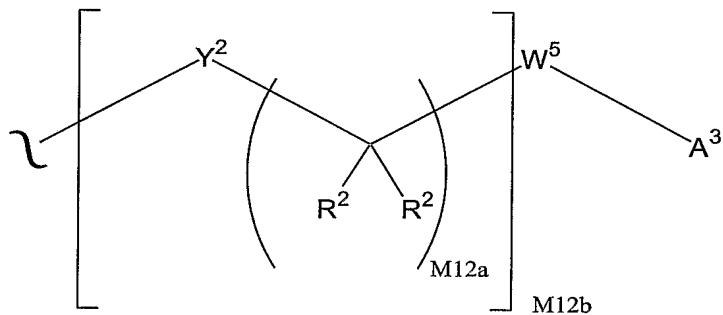


and  $W^{5a}$  is a carbocycle or a heterocycle where  $W^{5a}$  is independently substituted with 0 or 1  $R^2$  groups.

5

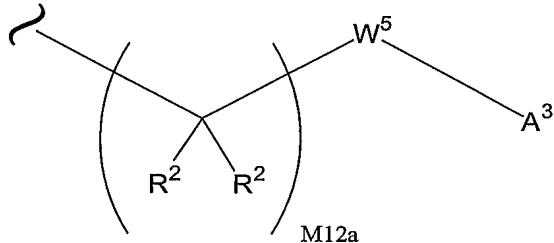
11. The compound of claim 5 wherein M12a is 1.

12. The compound of claim 5 wherein  $A^1$  is of the formula:

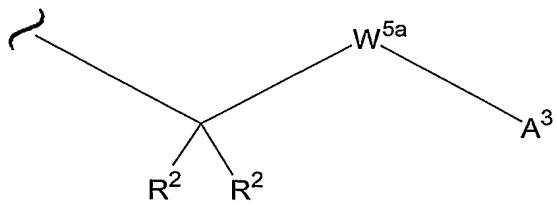


10

13. The compound of claim 5 wherein  $A^1$  is of the formula:



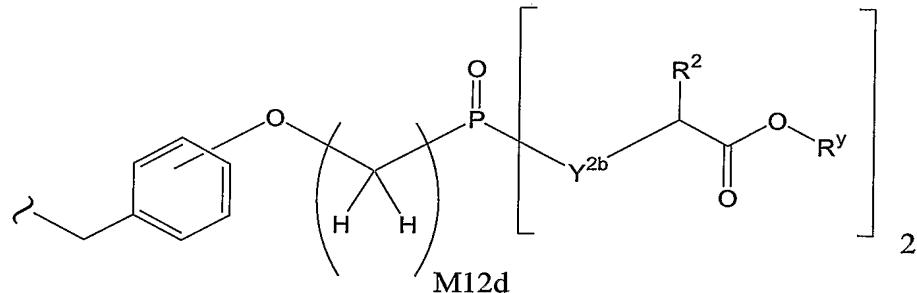
14. The compound of claim 5 wherein  $A^1$  is of the formula:



15

$W^{5a}$  is a carbocycle independently substituted with 0 or 1  $R^2$  groups;

15. The compound of claim 5 wherein  $A^1$  is of the formula:



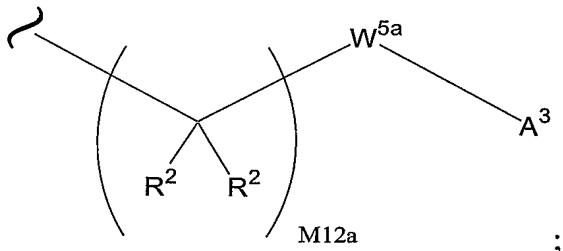
5

$Y^{2b}$  is O or  $N(R^2)$ ; and

$M12d$  is 1, 2, 3, 4, 5, 6, 7 or 8.

16. The compound of claim 5 wherein  $A^1$  is of the formula:

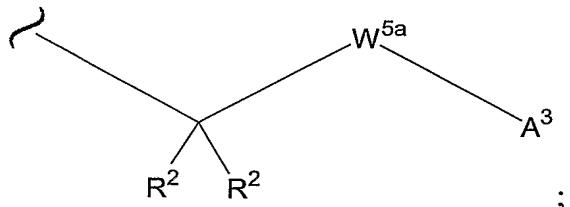
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$W^{5a}$  is a carbocycle independently substituted with 0 or 1  $R^2$  groups;

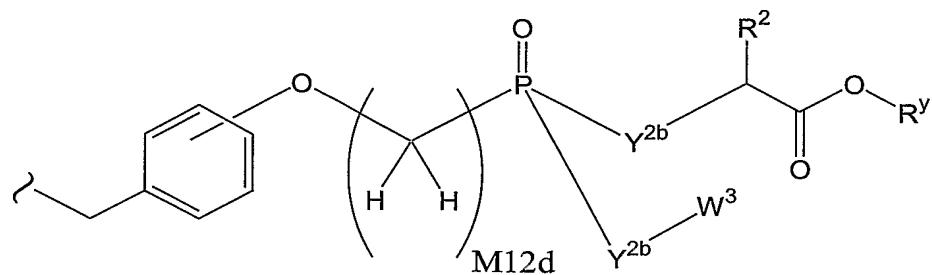
17. The compound of claim 5 wherein  $A^1$  is of the formula:

15



$W^{5a}$  is a carbocycle or heterocycle where  $W^{5a}$  is independently substituted with 0 or 1  $R^2$  groups.

20 18. The compound of claim 5 wherein  $A^1$  is of the formula:

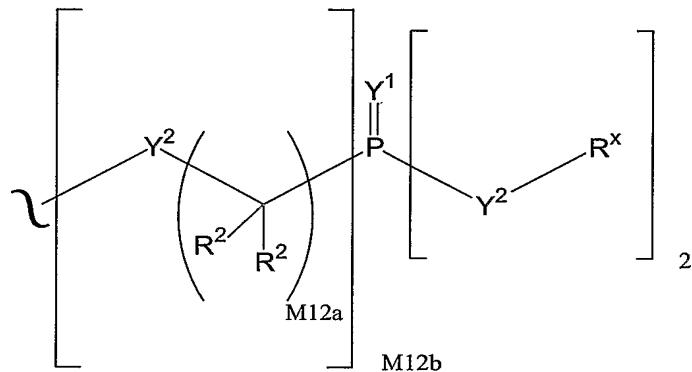


Y<sup>2b</sup> is O or N(R<sup>2</sup>); and

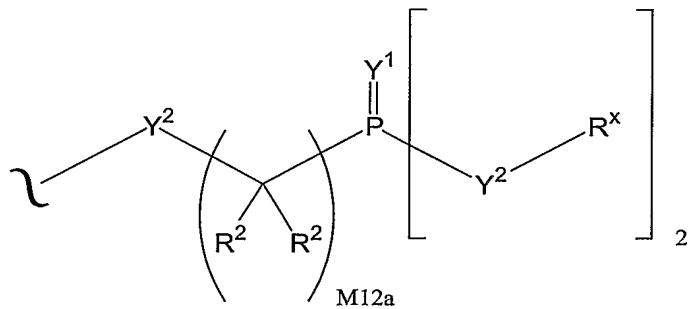
M12d is 1, 2, 3, 4, 5, 6, 7 or 8.

5

19. The compound of any one of claims 5-18 wherein A<sup>3</sup> is of the formula:

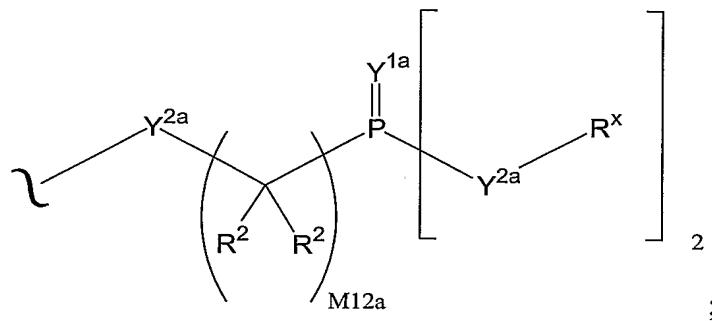


20. The compound of any one of claims 5-18 wherein A<sup>3</sup> is of the formula:



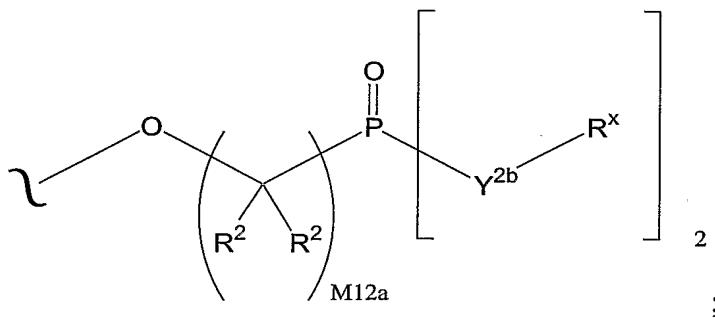
10

21. The compound of any one of claims 5-18 wherein A<sup>3</sup> is of the formula:



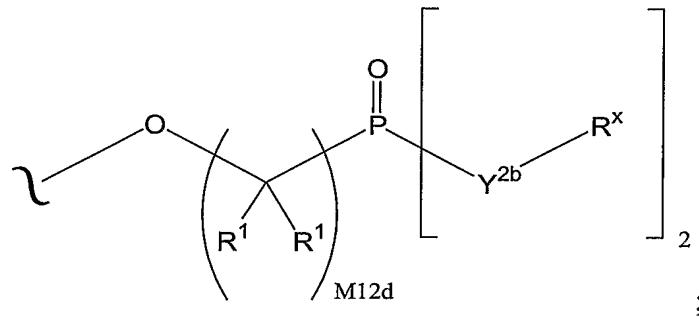
Y<sup>1a</sup> is O or S; and  
 Y<sup>2a</sup> is O, N(R<sup>x</sup>) or S.

5 22. The compound of any one of claims 5-18 wherein A<sup>3</sup> is of the formula:



and Y<sup>2b</sup> is O or N(R<sup>x</sup>).

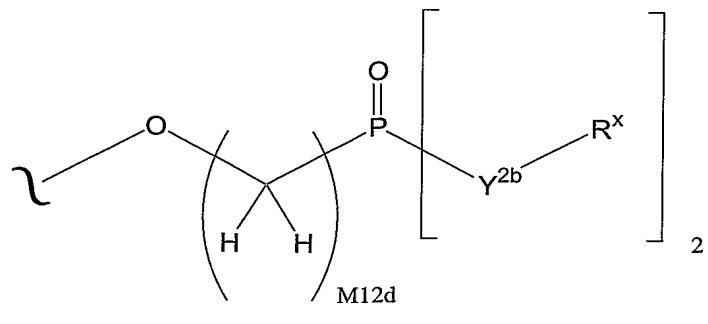
23. The compound of any one of claims 5-18 wherein A<sup>3</sup> is of the formula:



10

R<sup>1</sup> is independently H or alkyl of 1 to 18 carbon atoms;  
 Y<sup>2b</sup> is O or N(R<sup>x</sup>); and  
 M12d is 1, 2, 3, 4, 5, 6, 7 or 8.

15 24. The compound of any one of claims 5-18 wherein A<sup>3</sup> is of the formula:

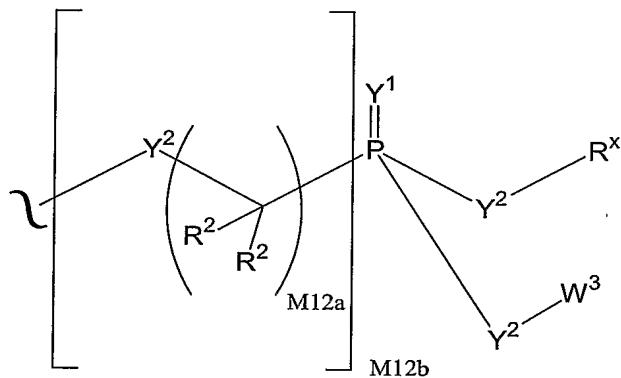


$Y^{2b}$  is O or  $N(R^x)$ ; and

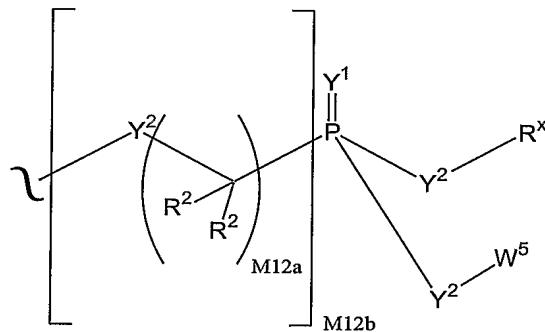
M12d is 1, 2, 3, 4, 5, 6, 7 or 8.

5 25. The compound of claim 24 wherein M12d is 1.

26. The compound of any one of claims 5-18 wherein  $A^3$  is of the formula:

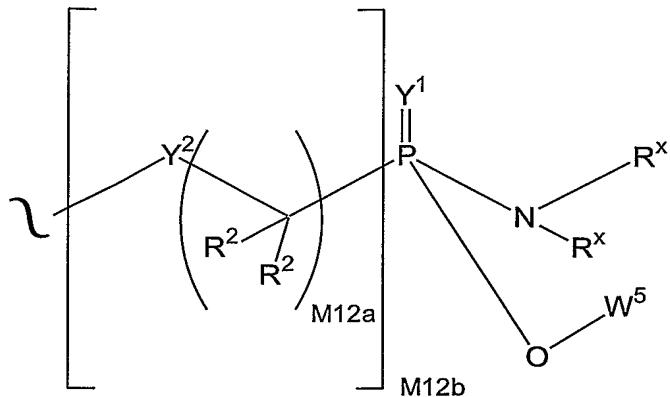


10 27. The compound of any one of claims 5-18 wherein  $A^3$  is of the formula:



28. The compound of claim 27 wherein  $W^5$  is a carbocycle.

29. The compound of any one of claims 5-18 wherein  $A^3$  is of the formula:

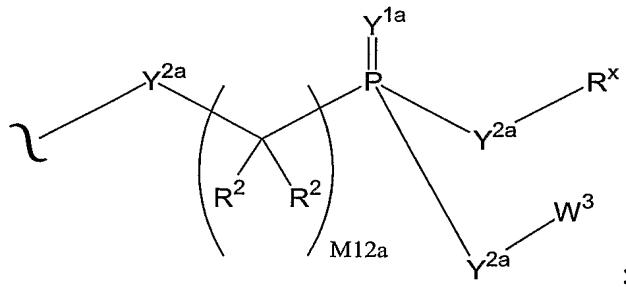


5 30. The compound of claim 29 wherein  $W^5$  is phenyl.

31. The compound of claim 30 wherein  $M12b$  is 1.

32. The compound of any one of claims 5-18 wherein  $A^3$  is of the formula:

10

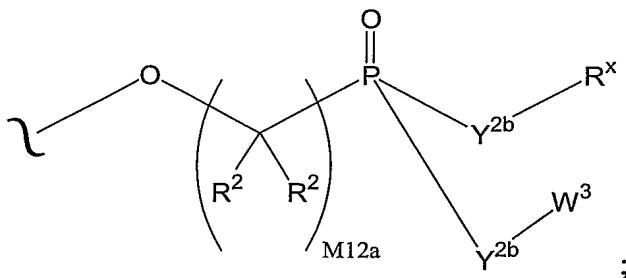


$Y^{1a}$  is O or S; and

$Y^{2a}$  is O, N( $R^x$ ) or S.

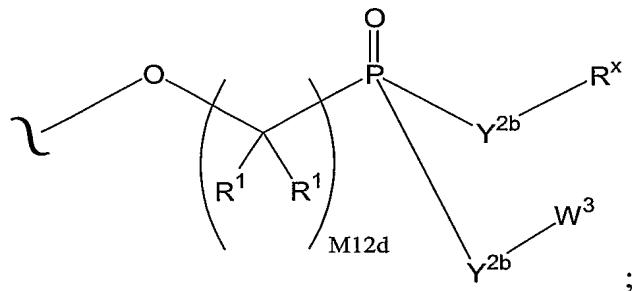
15 33. The compound of any one of claims 5-18 wherein  $A^3$  is of the formula:

15



and  $Y^{2b}$  is O or N( $R^x$ ).

34. The compound of any one of claims 5-18 wherein A<sup>3</sup> is of the formula:



R<sup>1</sup> is independently H or alkyl of 1 to 18 carbon atoms;

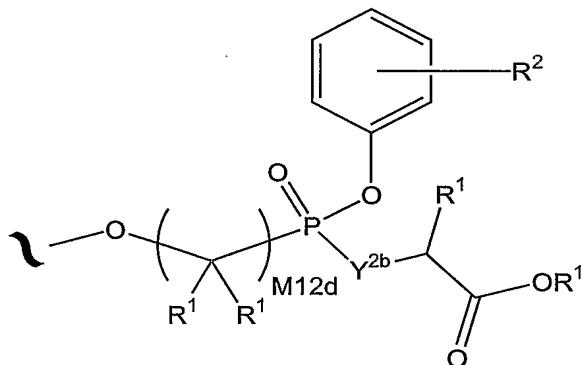
5 Y<sup>2b</sup> is O or N(R<sup>x</sup>); and

M12d is 1, 2, 3, 4, 5, 6, 7 or 8.

35. The compound of claim 34 wherein R<sup>1</sup> is H.

10 36. The compound of claim 34 wherein M12d is 1.

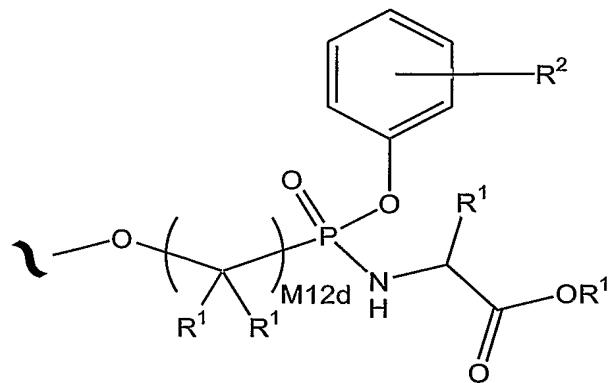
37. The compound of any one of claims 5-18 wherein A<sup>3</sup> is of the formula:



wherein the phenyl carbocycle is substituted with 0, 1, 2, or 3 R<sup>2</sup> groups.

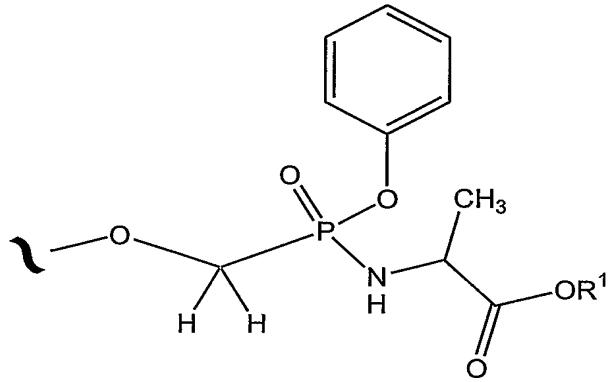
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38. The compound of any one of claims 5-18 wherein A<sup>3</sup> is of the formula:



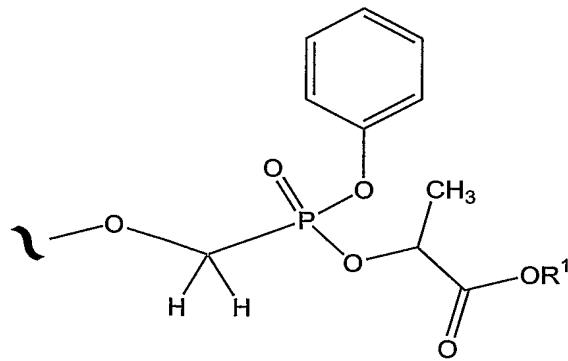
wherein R<sup>1</sup> is independently H or alkyl of 1 to 18 carbon atoms.

39. The compound of any one of claims 5-18 wherein A<sup>3</sup> is of the formula:

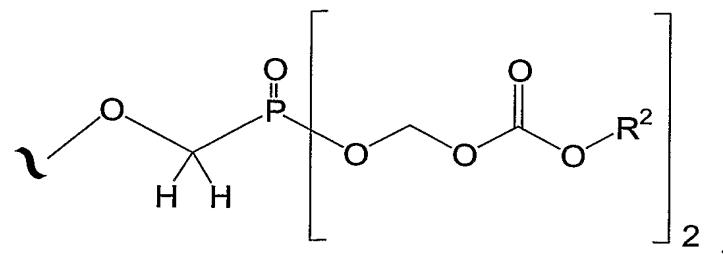


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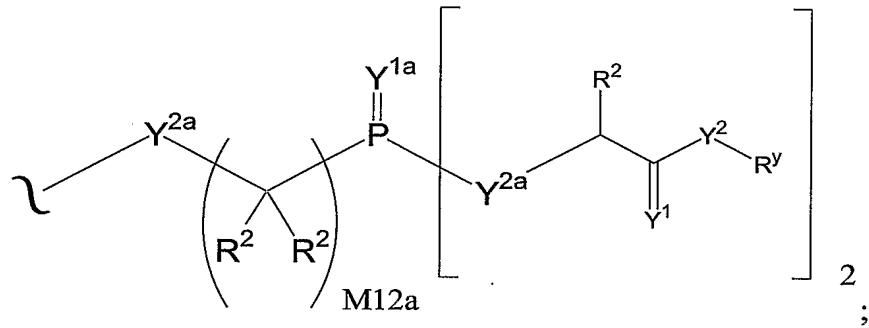
40. The compound of any one of claims 5-18 wherein A<sup>3</sup> is of the formula:



10 41. The compound of any one of claims 5-18 wherein A<sup>3</sup> is of the formula:



42. The compound of any one of claims 5-18 wherein  $\text{A}^3$  is of the formula:

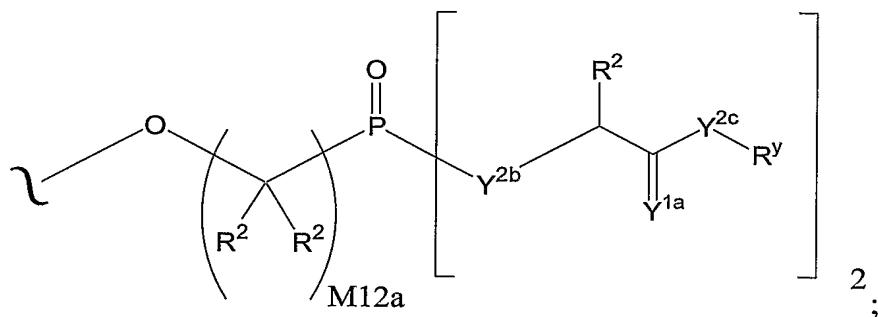


5

$\text{Y}^{1\text{a}}$  is O or S; and

$\text{Y}^{2\text{a}}$  is O, N( $\text{R}^2$ ) or S.

43. The compound of any one of claims 5-18 wherein  $\text{A}^3$  is of the formula:



10

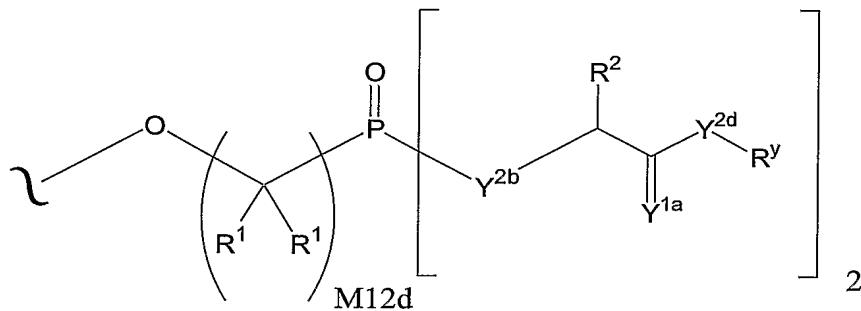
$\text{Y}^{1\text{a}}$  is O or S;

$\text{Y}^{2\text{b}}$  is O or N( $\text{R}^2$ ); and

$\text{Y}^{2\text{c}}$  is O, N( $\text{R}^y$ ) or S.

15

44. The compound of any one of claims 5-18 wherein  $\text{A}^3$  is of the formula:



$R^1$  is independently H or alkyl of 1 to 18 carbon atoms;

$Y^{1a}$  is O or S;

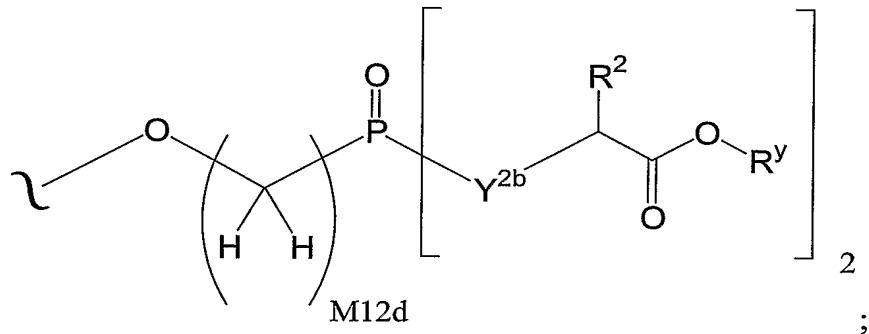
$Y^{2b}$  is O or  $N(R^2)$ ;

$Y^{2d}$  is O or  $N(R^y)$ ; and

5

M12d is 1, 2, 3, 4, 5, 6, 7 or 8.

45. The compound of any one of claims 5-18 wherein  $A^3$  is of the formula:

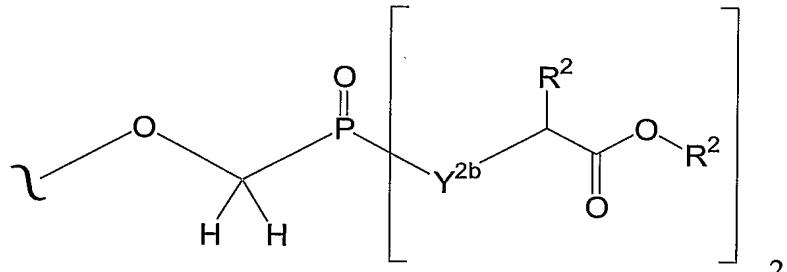


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$Y^{2b}$  is O or  $N(R^2)$ ; and

M12d is 1, 2, 3, 4, 5, 6, 7 or 8.

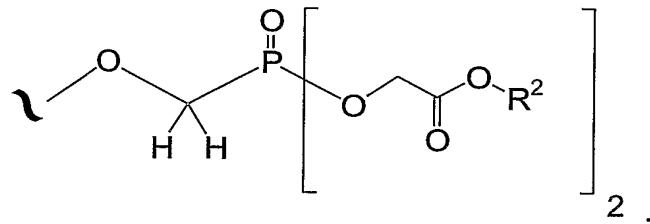
46. The compound of any one of claims 5-18 wherein  $A^3$  is of the formula:



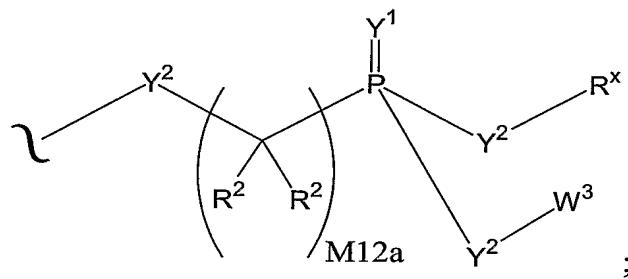
15

and  $Y^{2b}$  is O or  $N(R^2)$ .

47. The compound of any one of claims 5-18 wherein A<sup>3</sup> is of the formula:

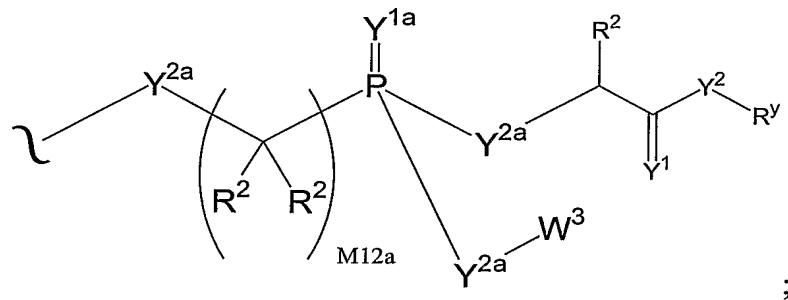


5 48. The compound of any one of claims 5-18 wherein A<sup>3</sup> is of the formula:



49. The compound of any one of claims 5-18 wherein A<sup>3</sup> is of the formula:

10

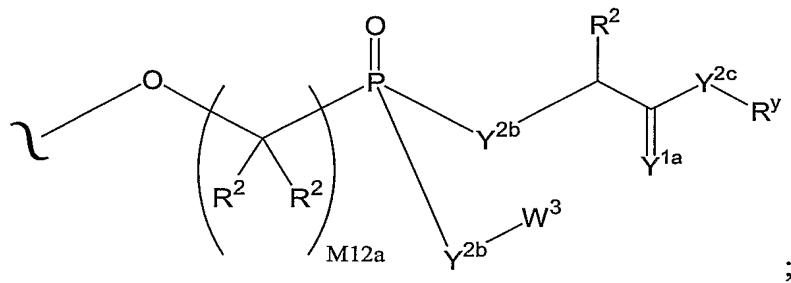


Y<sup>1a</sup> is O or S; and

Y<sup>2a</sup> is O, N(R<sup>2</sup>) or S.

50. The compound of any one of claims 5-18 wherein A<sup>3</sup> is of the formula:

15



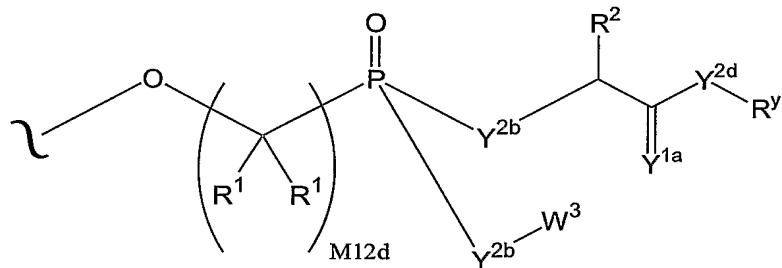
$Y^{1a}$  is O or S;

$Y^{2b}$  is O or  $N(R^2)$ ; and

$Y^{2c}$  is O,  $N(R^y)$  or S.

5

51. The compound of any one of claims 5-18 wherein  $A^3$  is of the formula:



$R^1$  is independently H or alkyl of 1 to 18 carbon atoms;

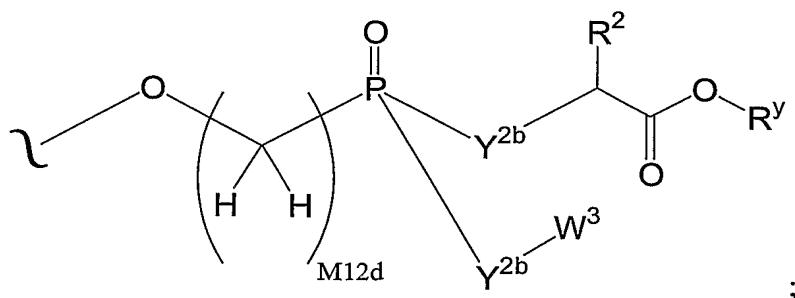
10  $Y^{1a}$  is O or S;

$Y^{2b}$  is O or  $N(R^2)$ ;

$Y^{2d}$  is O or  $N(R^y)$ ; and

M12d is 1, 2, 3, 4, 5, 6, 7 or 8.

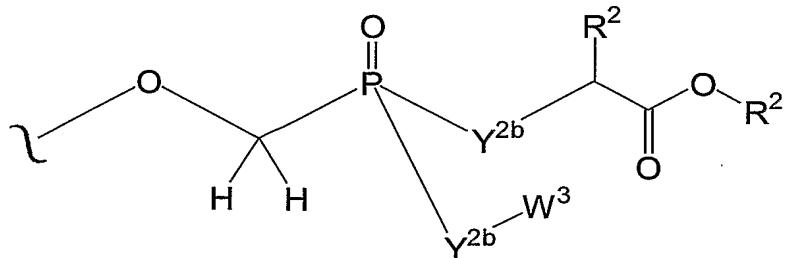
15 52. The compound of any one of claims 5-18 wherein  $A^3$  is of the formula:



$Y^{2b}$  is O or  $N(R^2)$ ; and

M12d is 1, 2, 3, 4, 5, 6, 7 or 8.

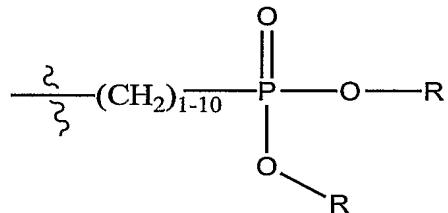
53. The compound of any one of claims 5-18 wherein A<sup>3</sup> is of the formula:



and Y<sup>2b</sup> is O or N(R<sup>2</sup>).

5

54. The compound of claim 5 wherein A<sup>0</sup> is of the formula:



wherein each R is independently (C<sub>1</sub>-C<sub>6</sub>)alkyl.

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55. The compound of claim 2 wherein:

R<sup>a</sup> is hydrogen, or substituted aryl;

R<sup>20</sup> is hydrogen, cycloalkyl, or -NR<sup>b</sup>R<sup>c</sup>;

R<sup>b</sup> is hydrogen, and R<sup>c</sup> is substituted alkyl, or substituted aryl;

15 R<sup>21</sup> is hydrogen, alkyl, substituted cycloalkyl, or substituted aralkyl;

R<sup>22</sup> is hydrogen, or alkyl; and

R<sup>23</sup> is hydrogen, substituted aryl, substituted cycloalkyl, or aralkyl.

56. The compound of any one of claims 1-55 which inhibits a  
20 serine/threonine kinase, tyrosine kinase, Bcr-Abl kinase, cyclin-dependent kinase, Flt3 tyrosine kinase, MAP Erk kinase, JAK3 kinase, VEGF receptor kinase, PDGF receptor tyrosine kinase, protein kinase C, insulin receptor tyrosine kinase, and/or an EGF receptor tyrosine kinase.

57. A pharmaceutical composition comprising a pharmaceutically acceptable excipient and a compound as described in any one of claims 1-55.

58. A unit dosage form comprising a compound as described in any one of  
5 claims 1-55 and a pharmaceutically acceptable excipient.

59. A method for inhibiting a kinase *in vitro* or *in vivo* comprising contacting a sample in need of such treatment with a compound as described in any one of claims 1-55.

10

60. The method of claim 59 wherein the contacting is *in vivo*.

61. A method of inhibiting a kinase in an animal, comprising administering a compound as described in any one of claims 1-55 to the animal.

15

62. The method of claim 61 wherein the compound is formulated with a pharmaceutically acceptable carrier.

63. The method of claim 62 wherein the formulation further comprises a  
20 second active ingredient.

64. The method of any one of claims 59-63 wherein the kinase is a serine/threonine kinase, tyrosine kinase, Bcr-Abl kinase, cyclin-dependent kinase, Flt3 tyrosine kinase, MAP Erk kinase, JAK3 kinase, VEGF receptor  
25 kinase, PDGF receptor tyrosine kinase, protein kinase C, insulin receptor tyrosine kinase, and/or an EGF receptor tyrosine kinase.

65. A method of treating cancer in an animal in need of such treatment comprising administering an effective amount of a compound as described in  
30 any one of claims 1-55 to the animal.

66. A compound as described in any one of claims 1-55 for use in medical therapy.
67. The use of a compound as described in any one of claims 1-55 to prepare  
5 a medicament for inhibiting a kinase in an animal.
68. The use of claim 67 wherein the kinase is a serine/threonine kinase,  
tyrosine kinase, Bcr-Abl kinase, cyclin-dependent kinase, Flt3 tyrosine kinase,  
MAP Erk kinase, JAK3 kinase, VEGF receptor kinase, PDGF receptor tyrosine  
10 kinase, protein kinase C, insulin receptor tyrosine kinase, and/or an EGF  
receptor tyrosine kinase.
69. The use of a compound as described in any one of claims 1-55 to prepare  
a medicament for treating cancer in an animal.  
15
70. A method for preparing a compound as described in the schemes and  
examples herein.
71. A method for preparing a pharmaceutical composition, comprising  
20 combining a pharmaceutically acceptable excipient and a compound as  
described in any one of claims 1-55.